Specified Substances

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Organizing Information

- FDA has the most important repository of human biological and product data but little integration.
  - Submission process
    - Paper
    - PDF's
  - Organizational
    - Different Centers
    - Different Contractors
    - Business Processes

SRS Integration

- Five essential levels to organize information at FDA
  - Substances
  - Products
  - Uses/biology/properties (Efficacy, Safety)
  - Submissions (Preapproval/Postapproval)
  - Manufacturers/Marketer/Sites
- Data should be linked to all information levels

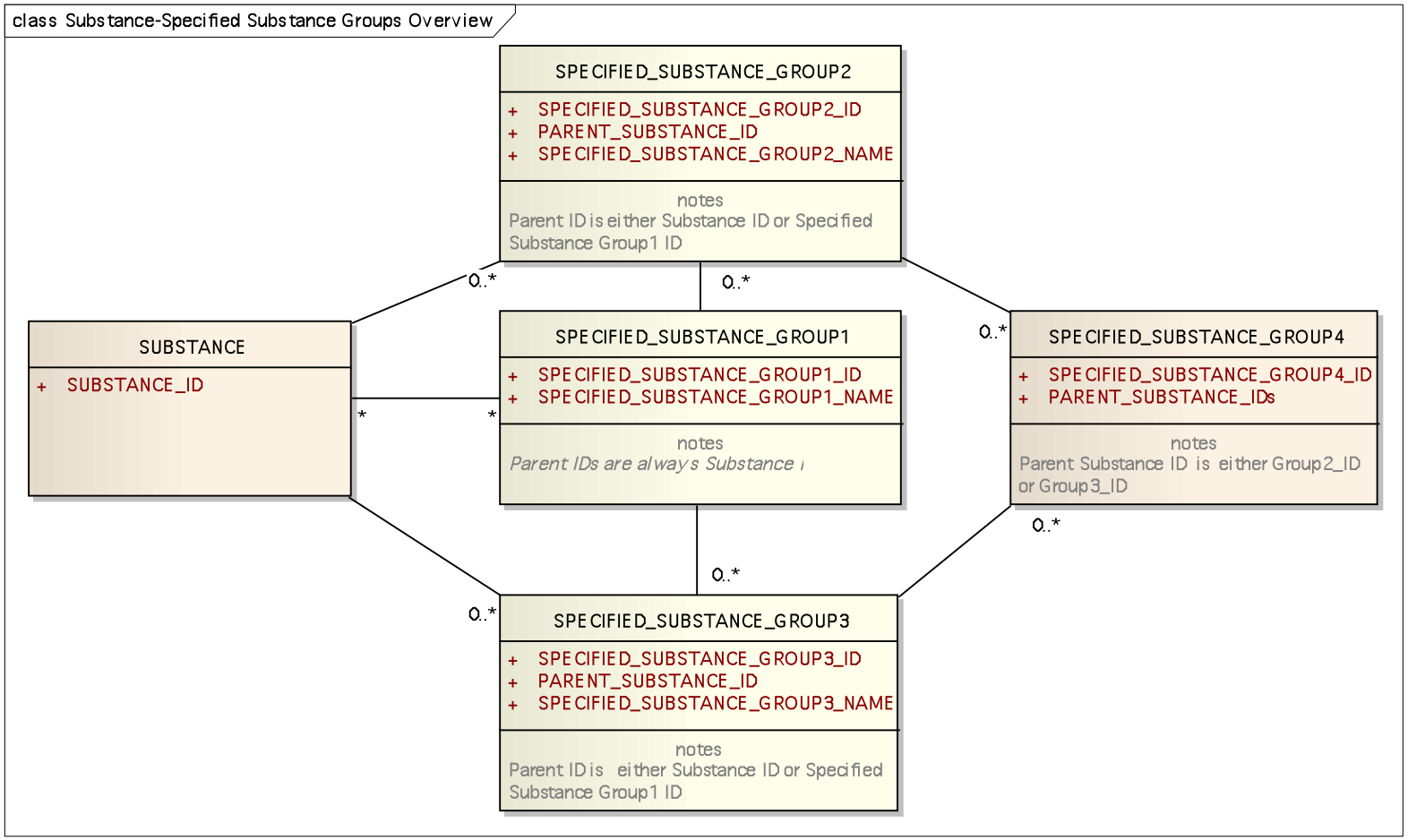
SRS Integration

- Data That Should be Linked Substances
  - LADMER
  - Targets
  - Metabolites
  - Constituents of Complex Materials
  - Specifications
  - Physical and Biological Properties
  - Environmental Fate
  - Uses
  - Toxicological, Animal, and Clinical Studies
  - ICSRs (Safety Reports)
  - Manufacturers, Sites, and Manufacturing Data
- Both Internal and External Links

Specified Substance

– An explicit grouping of elements and concepts is put forward in ISO not yet implemented in SRS but very useful for regulatory purposes
  - Group-1 Multiple substance materials, physical form, constituents and amount, extracts allergenic and herbal.
  - Group-2 Manufacturer and minimal manufacturing information
  - Group-3 Grade of material (USP, EP, technical, standardized etc.)
  - Group-4 Detailed manufacturing information, impurities, degradents etc.

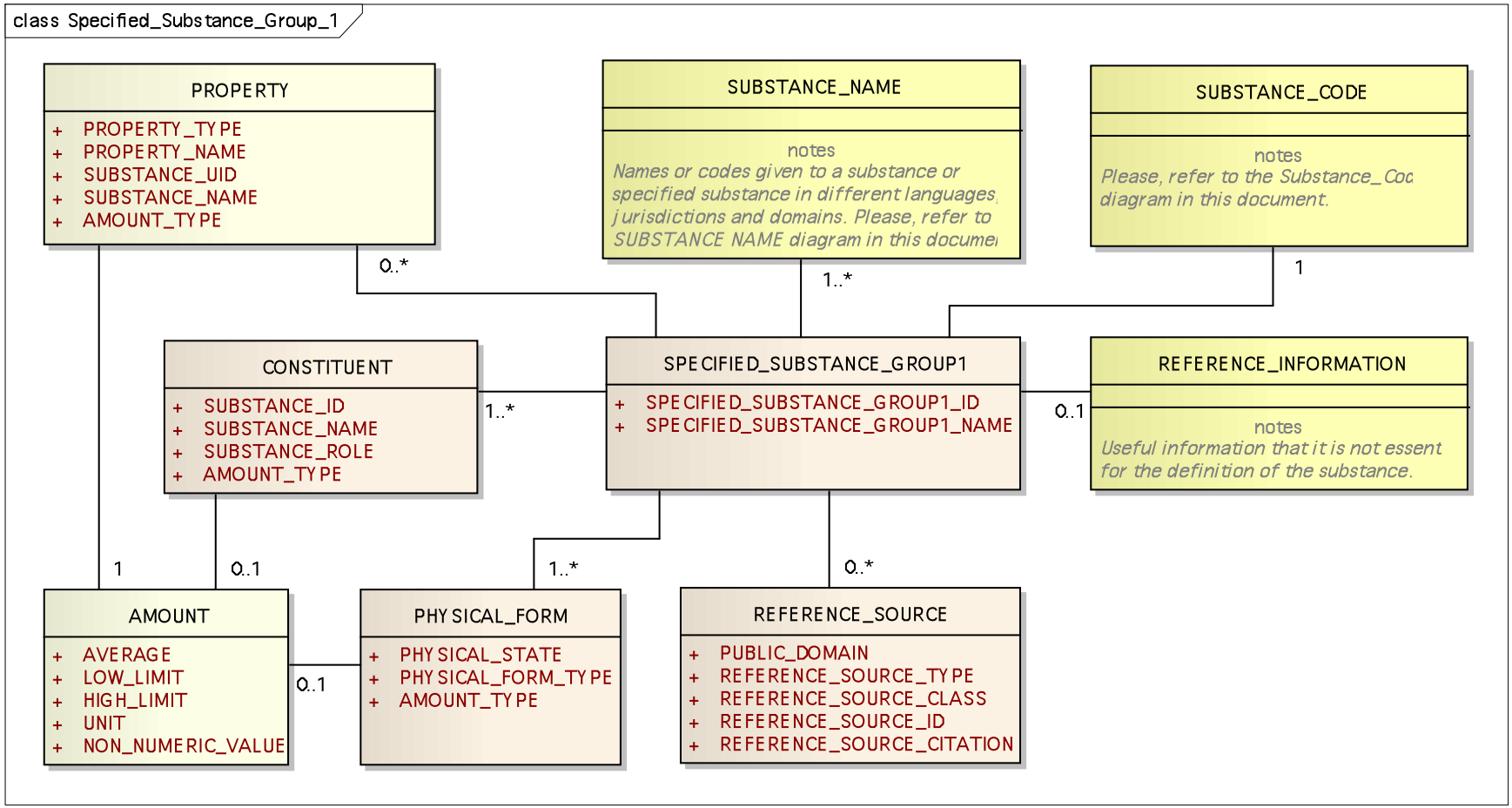
Substance -Specified Substance



Specified Substance

- Not yet implemented at FDA
- Each group will have an ID
  - Group-1 UNII
  - Group-2 Combination of Manufacturer and Substance ID
  - Group-3 Combination of Grade and Substance ID
  - Group-4 Group 2 with versioning

Group I Specified Substance

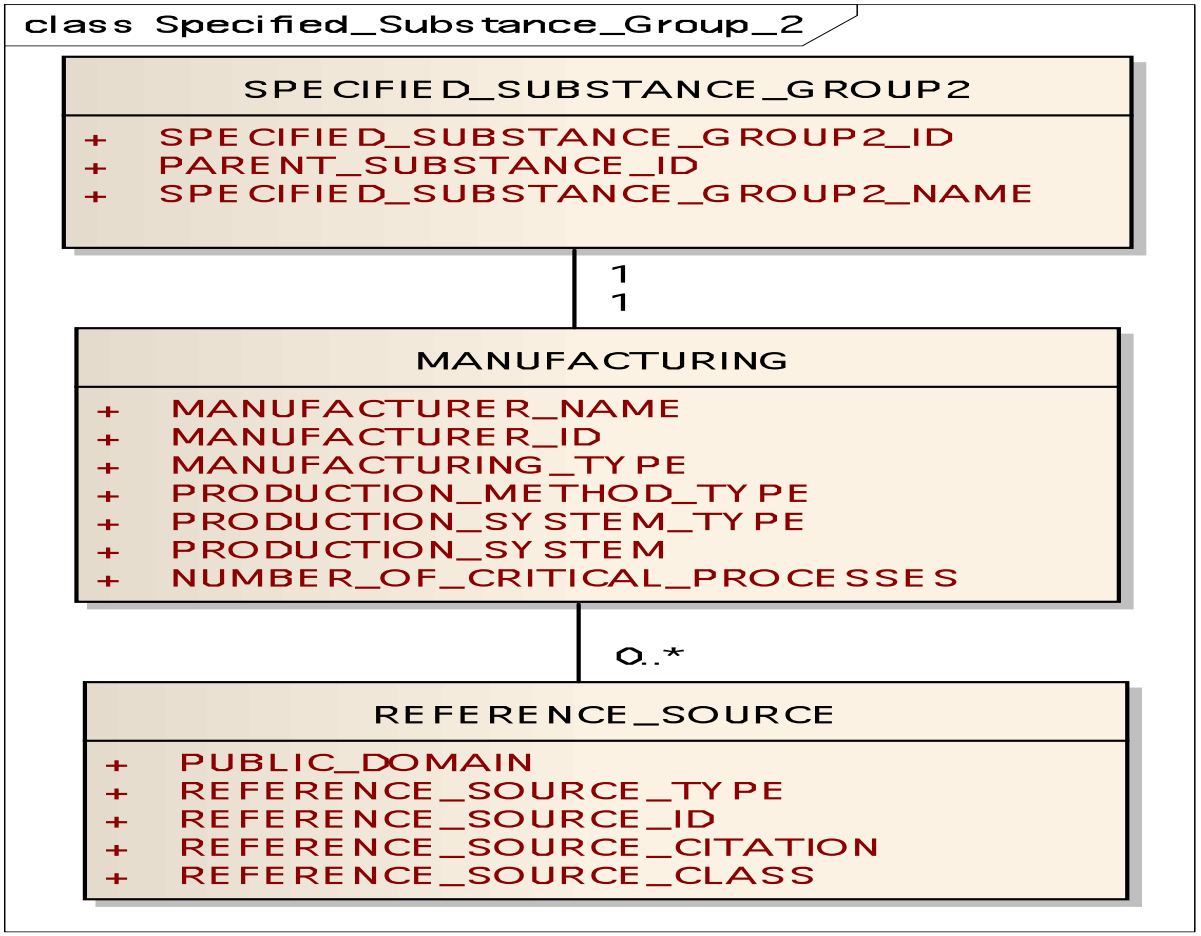


Group I Specified Substance

- Physical Form/Property
  - Distinguish Polymorphs/Crystalline and Amorphous
  - Further Distinguish Microcrystalline Celluloses

- Constituents
  - Create IDs for multiple substance materials
    - Simethicone/Isophane Insulins
  - Better Define Extracts Quantitative Values

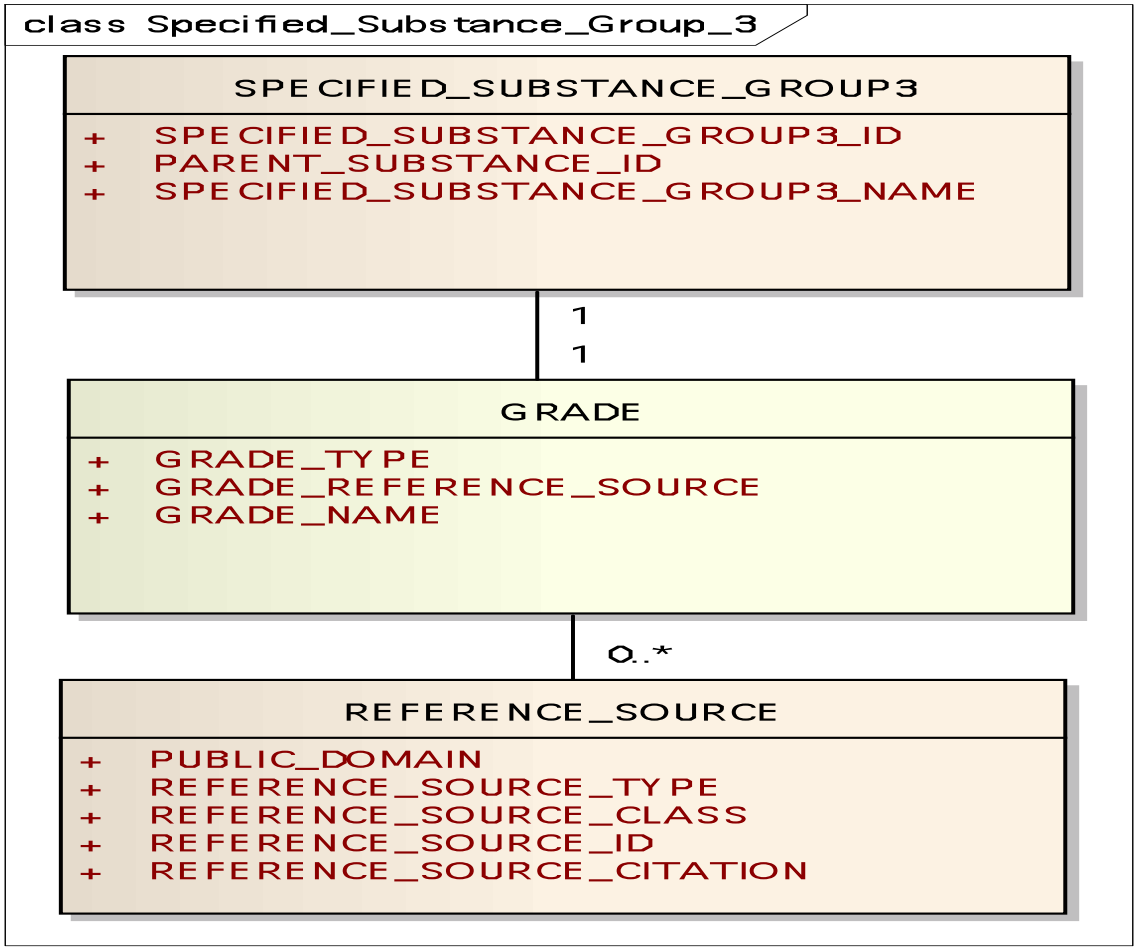
Group II Specified Substance



Group II Specified Substance

- Manufacturer
  - Ties Substance and/or Group I Specified Substance to a Manufacturer
  - Capture minimal manufacturing/marketing information
  - What is manufacturing
    - Repackaging?
    - Capture previous manufacturer?
    - Marketer
  - How will manufacturers be identified (DUNS country registrations systems.
- Production System
  - Biosimilars Cell lines
  - What changes in Critical Process would trigger a new ID

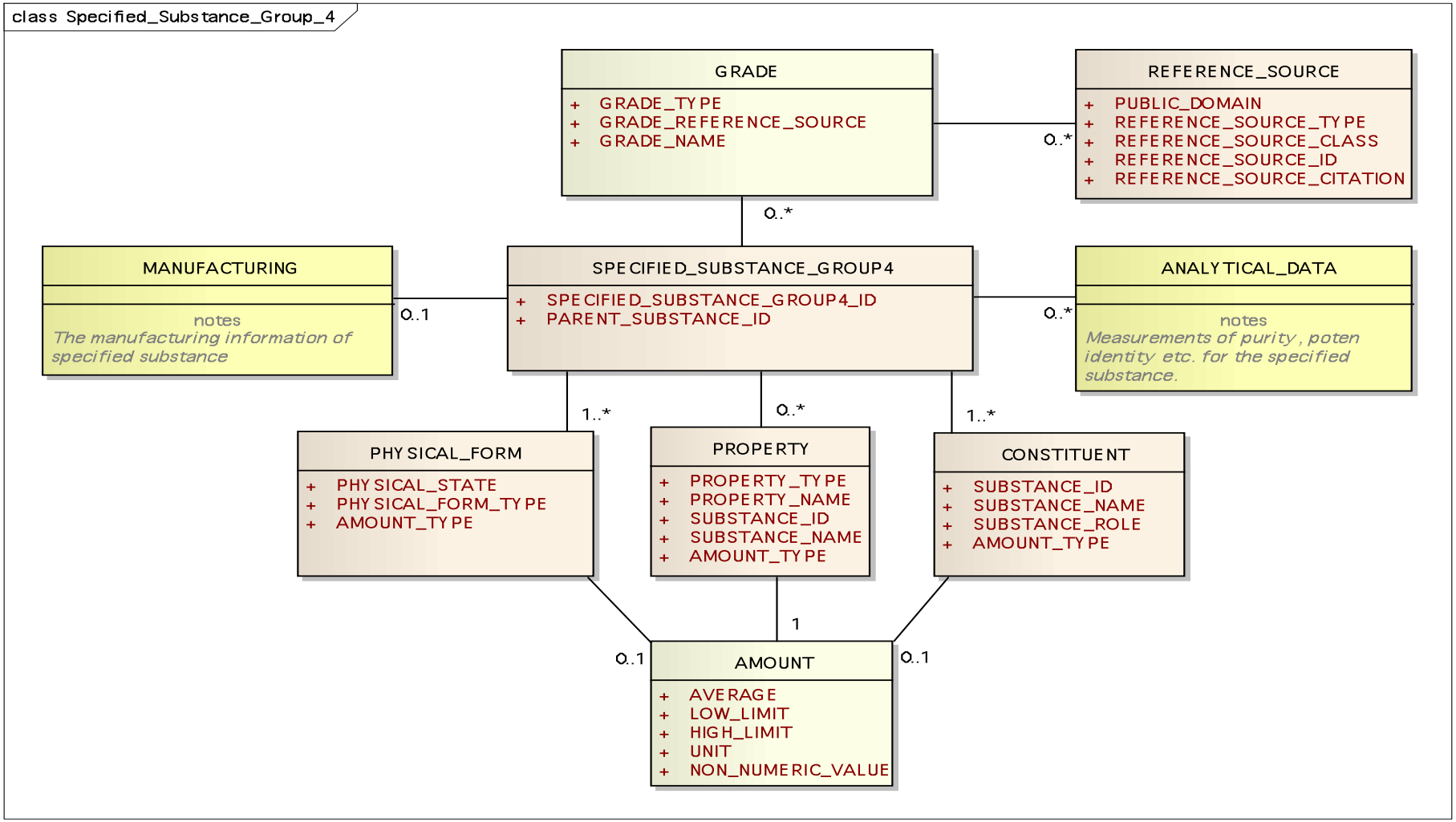
Group III Specified Substance



Group III Specified Substance

- Grade
  - Ties Substance to a Specific Grade
    - Pharmacopeial/Technical Grades
    - What triggers a new ID
      - » A change in monograph?
    - Allow Manufacturer Grades?
    - Pharmacopeial specifications for impurities will be captured at this level.

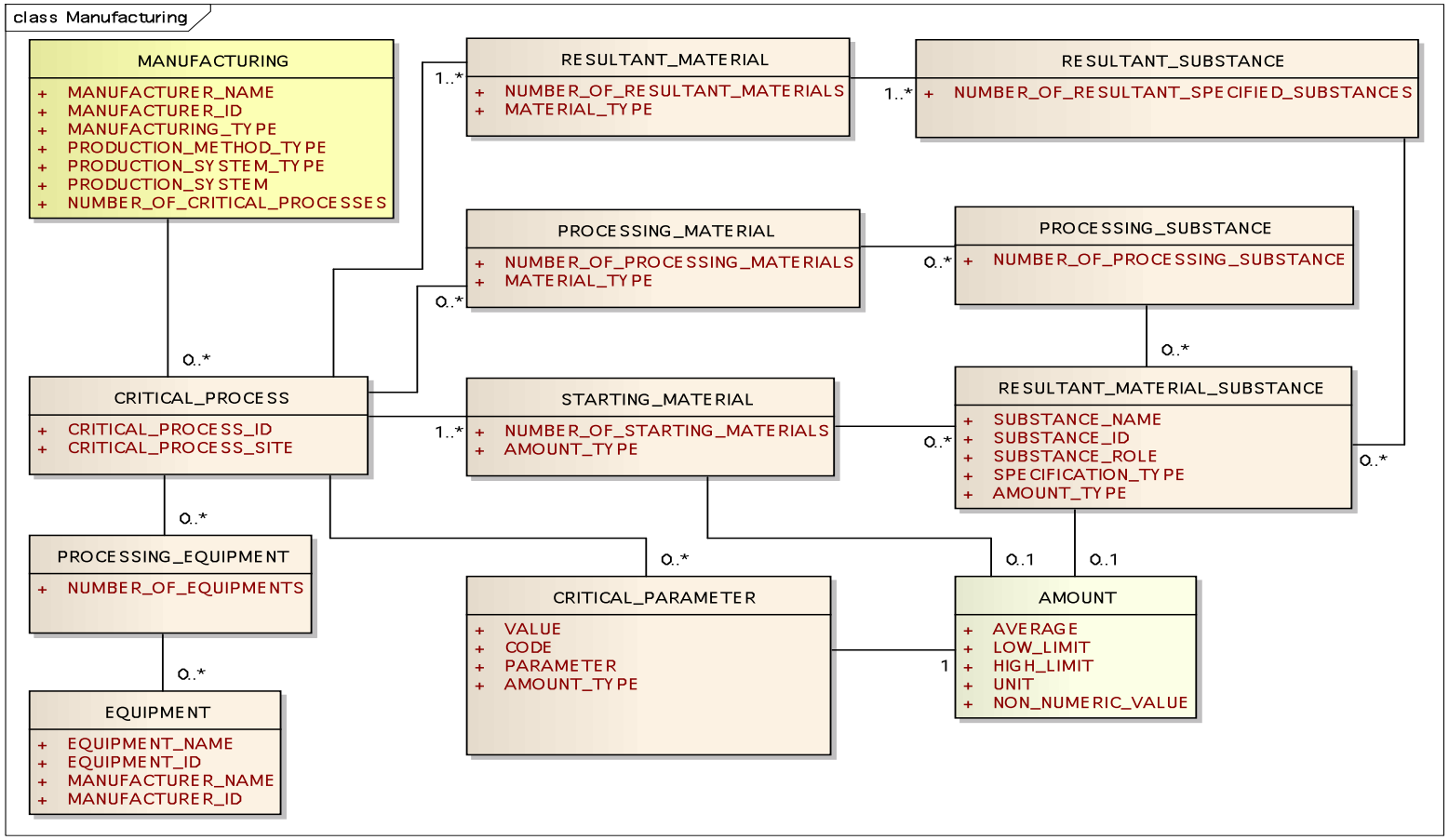
Group IV Specified Substance



Group IV Specified Substance

- Captured detailed manufacturing and specifications in a structured manner
  - Summary CMC section of eCTD
- Constituent
  - Link substances to impurities, degradents metabolites
    - Lot Data

Group IV Manufacturing Info

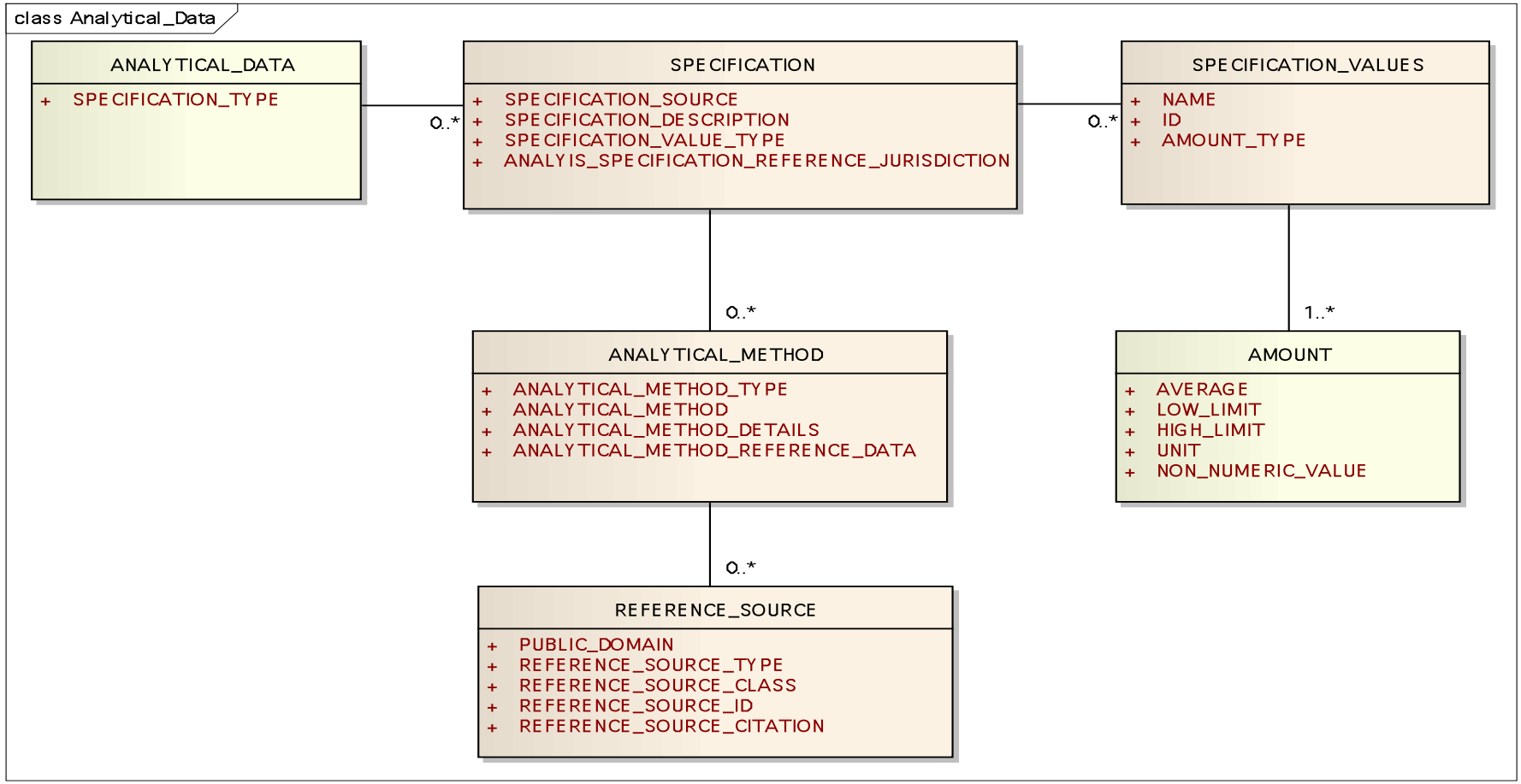


Group IV Manufacturing Info

Each Step In Manufacturing Process

- Starting Materials (Identified by Group II)
- Processing Materials (Identified by Group II)
- Resultant Materials
- Processing Equipment
- Critical Parameters

Group IV Analytical Data



Group IV Analytical Data

– A mechanism for capturing specifications for substances will be implemented in the second release
  - ID, Purity, Limit test, Assays, etc